## REMARKS

In the Office Action dated October 28, 2005, the Examiner rejected then pending Claims 38 and 40-43 under 35 U.S.C. §102(b) as allegedly anticipated by U.S. Patent No. 4,257,774 to Richardson et al. (hereinafter "Richardson").

Responsive to all rejections, Applicants have cancelled claims 39-41 without prejudice and amended claims 38 and 42-43.

Specifically, claim 38, from which claims 42-43 depend, has been amended to positively recite the detection of the "presence of micromolar amounts of a toxicant comprising a metal atom" and that the nucleic acid is "intercalated with a fluorescent dye." Support for such claim amendments can be found in the instant specification at Example 13 on page 22 and Example 5 on page 16.

Claim 38 has also been amended to delete the recitation "inhibition of binding of the dye to said nucleic acid molecule" to better delineate the method of the present invention as involving screening for <u>dissociation</u> of binding between the nucleic acid molecule and the fluorescent dye, rather than inhibition of binding.

Applicants' claimed method as recited by claims 38 and 42-43 distinguishes over the Richardson reference in at least the following aspects:

First, claims 38 and 42-43 recite a method that detects the presence of a toxicant comprising a metal ion by screening for the <u>dissociation</u> of binding between the nucleic acid molecule and the fluorescent dye that is only fluorescent when bound to the nucleic acid molecule. In contrast, the method disclosed by Richardson measures the <u>inhibition</u> (rather than dissociation) of binding between the nucleic acid and a fluorescence intercalator, such as acridine orange, by detecting a change in fluorescent polarization of acridine orange.

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Secondly, the claimed method of the present invention measures binding with a fluorophore that is only fluorescent when bound to the nucleic acid molecule, and not by fluorescence polarization as disclosed in Richardson.

Thirdly, Richardson does not disclose detection of the presence of a toxicant comprising a metal ion, as positively recited by claims 38 and 42-43 of the present application.

Finally and importantly, nothing in Richardson teaches or suggests that the method disclosed therein is able to detect micromolar amounts of a toxicant comprising a metal atom, as positively recited by claims 38 and 42-43 of the present application.

Therefore, claims 38 and 42-43 as amended herein patentably distinguish over the disclosure by Richardson. Applicants request withdrawal of rejections of claims 38 and 42-43 under 35 U.S.C. §102(b).

The Examiner's rejection of claim 39 under 35 U.S.C. §102(b) as allegedly anticipated by U.S. Patent No. 5,561,042 to Weis et al. (hereinafter "Weis") is moot in light of the cancellation of claim 39 herein.

In the October 28, 2005 Office Action, the Examiner rejected claims 44 and 45 under 35 U.S.C. §103(a) as allegedly obvious over Richardson and Weis in view of U.S. Patent No. 6,242,246 to Gold et al. (hereinafter "Gold).

Applicants respectfully traverse the Examiner's rejections of claims 44 and 45, for the following reasons:

Claims 44 and 45 depend from claim 38 and therefore also recite the detection of the presence of micromolar amounts of a toxicant comprising a metal atom by screening for the dissociation of binding between the nucleic acid molecule and the fluorescent dye.

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None of the cited references, either taken alone or together, discloses the detection of micromolar amounts of a toxicant comprising a metal atom by the dissociation of binding between a nucleic acid and a fluorescent dye.

Moreover, Gold is related to detection of molecules that form base pairs with immobilized DNA molecules. In contrast, the claimed method of the present invention as recited by claims 44 and 45 does not disrupt base pairing, but rather changes the structure to sufficiently perturb the fluorescence of the dye.

Therefore, claims 44 and 45 patentably distinguish over the cited references Richardson, Weis, and Gold. Applicants request withdrawal of rejection of claims 44-45 under 35 C.F.R.§103 (a).

Based on the foregoing, this case is in condition for allowance, which action is earnestly solicited.

Respectfully submitted,

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